

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of)	
)	
Pierre DRUILHE)	
)	Group Art Unit: 1645
Serial No.:10/774,602)	
)	Examiner: N.M. Minnifield
Filed: February 10, 2004)	
)	
For: PLASMODIUM FALCIPARUM ANTIGENS INDUCING PROTECTIVE ANTIBODIES		

1.132 DECLARATION

Hon. Commissioner of Patents
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Alexandria, Virginia
22313-1450

I, Pierre Druilhe do hereby declare the following:

[1] I am currently the director of the Biomedical Parasitology Unit at Institut Pasteur in Paris, France and have been the director of this department for many years. I have published 260 articles and have 10 U.S. Patents issued in my name. I am one of the inventors of the above-captioned U.S. patent application. Enclosed please find attached a copy of my *Curriculum Vitaè*.

[2] I have read the last U.S. Official Action dated March 25, 2005, for the above-identified patent application. It is my understanding that the Examiner deems that the claims directed to vaccines cannot be produced by a scientist using the disclosure of the above-captioned specification since the specification does not teach a scientist how to obtain a malaria vaccine. It appears that the Examiner's reasoning in

maintaining this rejection is that she deems that none of the claimed peptides either alone or in combination will protect against malaria. I respectfully disagree with the Examiner for the following reasons.

[3] MSP-3 is a polymorphic protein that binds to the merozoite surface and traffics to the parasitophorous vacuole. It has a molecular weight of 48 KD and is recognized by cytophilic antibodies IgG1 and IgG3 in protected subjects and non-cytophilic antibodies in unprotected subjects. This protein is further capable of inducing antibodies which cooperate with monocytes in the antibody-dependent cellular inhibition (ADCI) reaction. Within this protein, certain conformational epitopes are recognized by T lymphocytes. The present specification provides long synthetic peptides which have particular conformational epitopes recognized by T lymphocytes and B epitopes such as MSP-3a, MSP-3b, MSP-3c and MSP-3d. Furthermore, IFN- γ secretion in response to the LSP peptide was extremely high in the range of 10,000 to 50,000 International Units and remained high over the immunization process.

[4] Besides the overview presented above in paragraph (3), the present specification describes the isolation of the clone DG210. The characterization of the protein synthesized by this clone such as inducing an ADCI reaction *in vivo*, the study of lymphoproliferative responses, the sequencing and characterization of the genome clone, and the isotypic characteristics ; i.e., the protein is recognized preferentially by IgG1 and IgG3 in the blood of protected subjects is also described in the present invention.

[5] The study of the polymorphism of the gene and epitopes defined by the clone DG210 was also undertaken using two cultures of strains of African *P.falciparum*, of 4 Thai isolates and 29 African isolates. Screening by Western blot with 6 Thai or African isolates and indirect immunofluorescence of 10 isolates from the Congo confirmed that the epitopes are representative of non-polymorphic conserved regions. The results of these studies were also described in the specification.

[6] A phase I clinical study using a long synthetic peptide derived from MSP3 to evaluate the safety and tolerance of the vaccine, as well as the immunogenicity was disclosed in the specification. In this regard, 36 Swiss volunteers were administered

the synthetic peptide from MSP-3 with either Alum or Montanide® as an adjuvant. The long Synthetic Peptide formulation of MSP-3 was found to be safe and immunogenic. The antibodies that were induced were IgG1 and IgG3, which subclasses of antibodies bind to the Fc gamma receptors on monocytes, thus indicating the monocyte-dependent, antibody-mediated effect.

[7] Additional studies set forth in the specification show natural passive transfer of antibodies from mother to newborns, of IgG3 antibodies and that IgG anti MSP-3b antibodies strongly differentiated 2 groups. Studies were also undertaken in cerebral malaria patients. It should be recalled that cerebral malaria involves the clinical manifestations of *Plasmodium falciparum* malaria that induces mental status and coma. It is a disease of the brain that is accompanied by fever and has a 25% to 50% mortality rate. Ring-like lesions in the brain are major characteristics of this etiology.

[8] The results of a study in Niakhar with 4,200 children, which were sampled during the non-transmission season and followed during the transmission season was also described in the specification. 51 children acquired cerebral malaria, 9 of which died despite treatment. The 9 children that died had significantly lower titers of anti-MSP-3 antibodies compared with the 42 cerebral malaria children who survived and as further compared with 100 acute uncomplicated malaria cases. A similar study was conducted on patients in a hospital of Dakar except serum was taken upon admission. A significant difference was found in IgG3 antimalarial antibodies between survivors and individuals who passed away; i.e., lower titers of anti MSP-3 antibodies were found in those patients who passed away.

[9] Finally the specification discloses a SCID mouse model infected with *P. falciparum* and shows passive transfer in SCID mice.

[10] Besides, the disclosure in the specification additional studies were undertaken since the patent application was filed. The association of MSP-3 antibodies with protection against malaria was demonstrated in Dielmo with over 2 years of follow-up. In the Dielmo studies over 220 individuals of all ages were followed, as well as 62 pregnancies. Daily medical exams were given and sequential sera were taken (at least 88,000 sera samples) preceding a given malaria attack. It was also

demonstrated in Burma in an hyperendemic area and by immunization and challenge of Aotus monkeys.

[11] In fact, additional Western blots, and SGI% of the volunteers which were previously injected with 3 doses of MSP-3 long synthetic peptides in comparison with P1AG were taken after 1 year. Further measurements were made greater than 1 year after immunization of the MSP-3 LSP's of the present invention. The results of the first study are indicated in attached Annex I. As can be seen from these results and our further results of greater than one year, the immune response obtained after immunization was long-lasting. Furthermore, biological assays demonstrated that the induced antibodies can mediate protection against *P. falciparum*.

[12] Further results were undertaken in a volunteer that was Western blot positive and administered the MSP-3 LSP's of the present invention. As can be seen in enclosed Annex II, after 12 months post immunization, the parasitemia dropped to 0.01 % on day 30.

[13] Thus, in view of paragraphs [2] to [12] above, the conclusions that can be made are the following:

(a) that MSP3-LSP's set forth in the present invention provide a malaria vaccine that is safe, well tolerated when adjuvated with alum or Montanide® and are able to elicit antibodies in humans that are able to kill *P. falciparum*;

(b) even low doses of MSP3 LSP's injected with simple adjuvants induce long-lasting antibodies of the cytophilic classes;

(c) the MSP3 LSP's of the present invention are directed to fully conserved epitopes and have a strong biological effect against *P. falciparum*; and

(d) the antibodies elicited in volunteers, after injection of the MSP-3 long synthetic proteins of the present invention, were able to inhibit parasite growth both *in vivo* and *in vitro* via the antibody-dependent monocyte-mediated mechanism.

[14] It appears that the Examiner has taken a strict interpretation of the word "vaccine" since at page 7 of the Official Action, the Examiner states that "none of these are clearly indicative that the claimed peptides either alone or in combination will protect against malaria. An immune response is not protection against malaria."

However, it is well known by scientists in this field that the goal of erythrocytic malaria vaccines is either to reduce the parasite load by preventing invasion of red cells or to prevent parasite replication and/or growth after invasion of the parasite. In this regard the present invention provides a mechanism to block the *P. falciparum* parasite as demonstrated in the specification. Thus the result of the ADCl experiments, which is a mechanism mediated by soluble components released by monocytes that block the division of intraerythrocytic parasites, is a clear indication of parasite killing. Indeed, ADCl can provide a means of generating cross-strain protection, since macrophages activated by antibodies to one variant can kill parasites in red blood cells of other strains and variants of *P. falciparum*. Moreover ADCl can continue after merozoite invasion and entry into the red blood cells.

[15] In view of paragraphs [1] to [14], it can only be concluded that a scientist in this field can gather from the contents of the specification that malaria vaccines can be produced by a scientist using the disclosure of the above-captioned specification

I also declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

27-05-2005

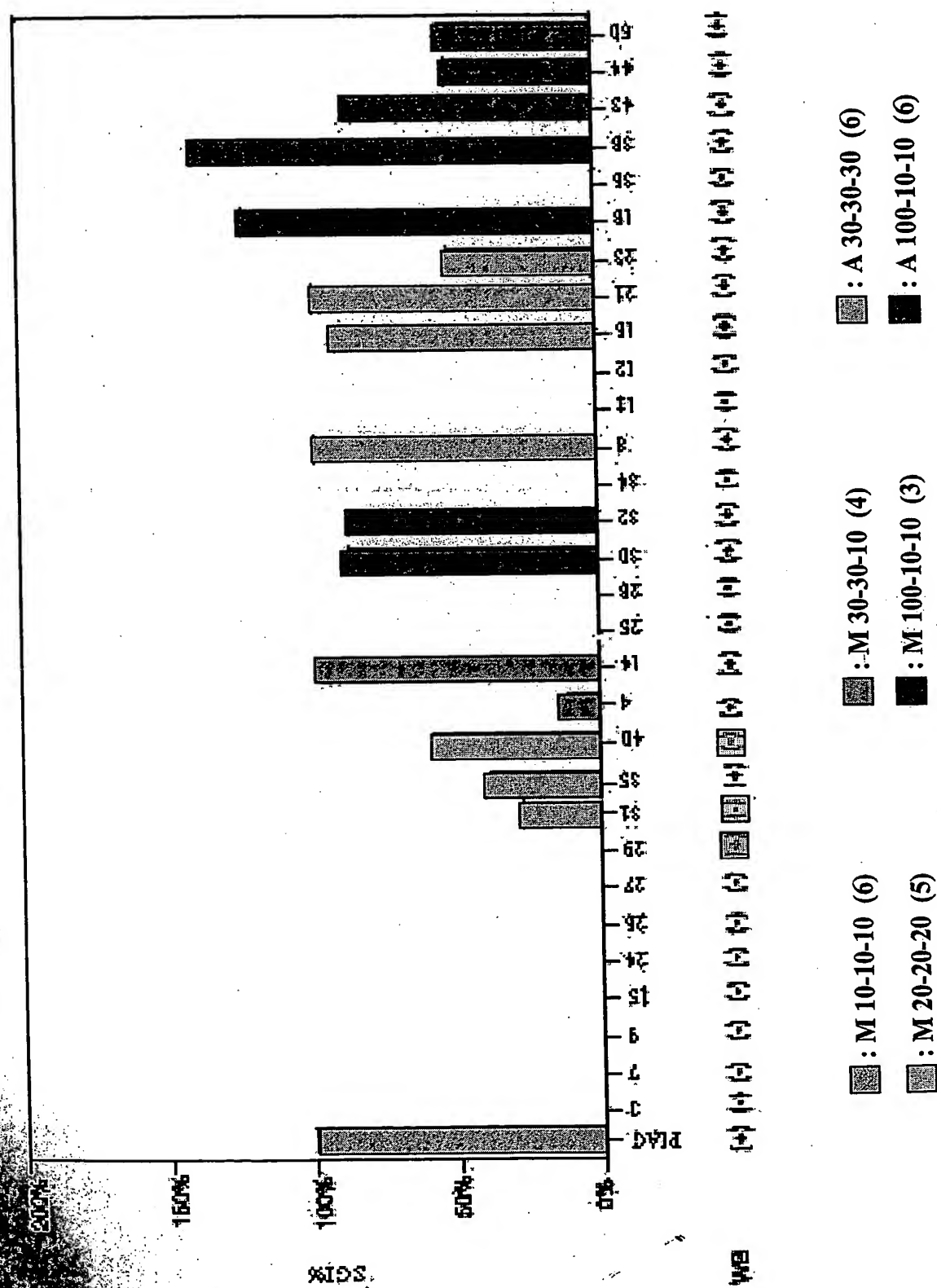
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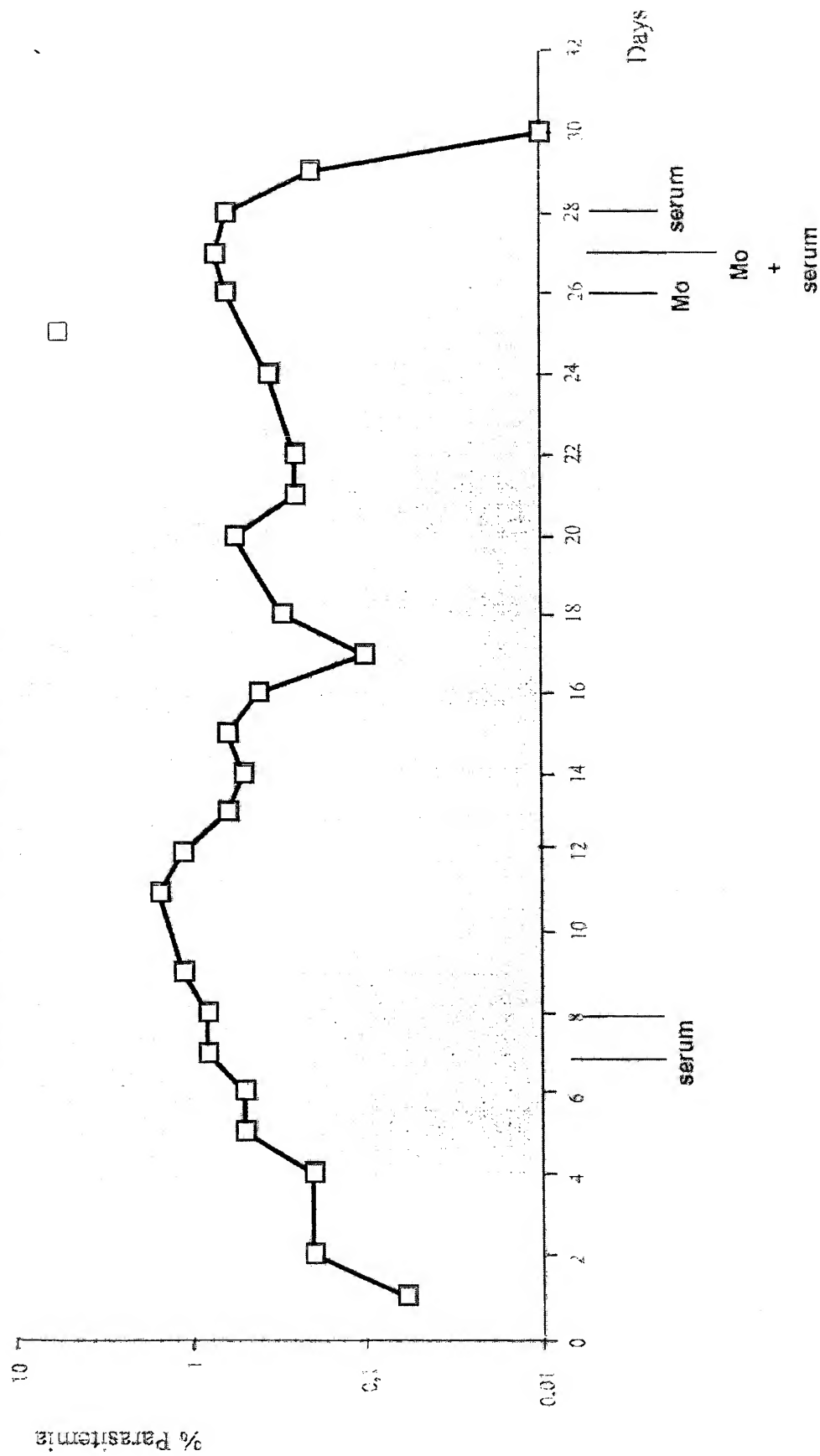
Pierre DRUILHE

Western blot result and SGP% of the volunteers one year after 3 doses of MSP3

Long Synthetic Peptide Immunization in comparison with PLAG.



Volunteer 18, 12 months post-immunisation, WB+



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1972 - Medical Degree, Paris University
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Ss-Dossier 224531 FR 01 AMTIG. HEPATIQUE P FALCIPARUM				Inventeur: DRU002 DRUILLE PIERRE	
N° D.I 186028 ANTIGENES HEPATIQUE DE P. FALCIPARUM					
N° Ss-Dossier Pays	N° Dépôt	Date Dépôt	Type de lien	Co-Propriétaire 1	Co-Propriétaire 2 Co-Propriétaire 3
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224531 AT 01 AUTRICHE	EU889018545	9/02/1988		INSTITUT PASTEUR	CNRS
224531 AU 01 AUSTRALIE	AU1342888	9/02/1988		INSTITUT PASTEUR	CNRS
224531 BE 01 BELGIQUE	EU889018545	9/02/1988		INSTITUT PASTEUR	CNRS
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224531 JP 01 JAPON	JP501827	9/02/1988		INSTITUT PASTEUR	CNRS
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224531 PC 01 PCT	ECTPR8800074	9/02/1988		INSTITUT PASTEUR	CNRS
224531 US 01 ETATS-UNIS	US275139	9/02/1988		INSTITUT PASTEUR	P.M.S.V.
224531 US 02 ETATS-UNIS	US462512	7/06/1995	Division	INSTITUT PASTEUR	CNRS
224531 US 03 ETATS-UNIS	US462062	7/06/1995	Division	INSTITUT PASTEUR	CNRS
224531 US 04 ETATS-UNIS	US760000	3/12/1996	Division	INSTITUT PASTEUR	CNRS
Ss-Dossier 224532 FR 01 ANTIGENES SPOROZOITE-HEPATIQUE				Inventeur: DRU002 DRUILLE PIERRE	
N° D.I 189011 ANTIGENES DE SPOROZOITE DE P. FALCIPARUM					
N° Ss-Dossier Pays	N° Dépôt	Date Dépôt	Type de lien	Co-Propriétaire 1	Co-Propriétaire 2 Co-Propriétaire 3
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224532 AU 01 AUSTRALIE	AU5315790	11/04/1990		INSTITUT PASTEUR	CNRS
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224532 NZ 01 NZL. ZELAND	NZ233328	12/04/1990		INSTITUT PASTEUR	CNRS
224532 PT 01 PORTUGAL	PT93764	12/04/1990		INSTITUT PASTEUR	CNRS
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224532 US 02 ETATS-UNIS	US758724	9/09/1991	Contin° in Part	INSTITUT PASTEUR	CNRS
224532 US 03 ETATS-UNIS	US104597	10/08/1993		INSTITUT PASTEUR	CNRS
224532 US 04 ETATS-UNIS	US242060	13/05/1994	Contin° in Part	INSTITUT PASTEUR	CNRS
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224532 US 06 ETATS-UNIS	US EN ATTEMTE	18/03/1999	Continuation	INSTITUT PASTEUR	CNRS
224532 ZA 01 AFRQ-SUD	ZA902831	12/04/1990		INSTITUT PASTEUR	CNRS
Ss-Dossier 233621 FR 01 EPI TOPE T DE P. FALCIPARUM				Inventeur: DRU002 DRUILLE PIERRE	
N° D.I 190014 EPI TOPE T DE P. FALCIPARUM					
N° Ss-Dossier Pays	N° dépôt	Date dépôt	Type de lien	Co-Propriétaire 1	Co-Propriétaire 2 Co-Propriétaire 3
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233621 GB 01 GR. BRETAG.	EU929058972	5/02/1992		INSTITUT PASTEUR	CNRS
233621 GR 01 GRECE	EU929058972	5/02/1992		INSTITUT PASTEUR	CNRS
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233621 US 01 ETATS-UNIS	US0983137	5/02/1992	INSTITUT PASTEUR	CNRS
233621 US 02 ETATS-UNIS	US462625	7/06/1995 Division	INSTITUT PASTEUR	CNRS
233621 US 03 ETATS-UNIS	US837344	19/04/2001 Division	INSTITUT PASTEUR	CNRS
233621 US 04 ETATS-UNIS	US900963	10/07/2001 Division	INSTITUT PASTEUR	CNRS

Ss-Dossier 250068 FR 01 P48KD DE P. FALCIPARUM Inventeur: DRU002 DRUILHE PIERRE
N° D.I 192053 P48KD DE P. FALCIPARUM

N° Ss-Dossier	Pays	N° Dépot	Date Dépot	Type de lien	Co-Propriétaire 1	Co-Propriétaire 2	Co-Propriétaire 3
250068 AT 01 AUTRICHE	FR9212488	19/10/1992	INSTITUT PASTEUR				
250068 BE 01 BELGIQUE	EU939235842	18/10/1993	INSTITUT PASTEUR				
250068 CH 01 SUISSE	EU939235842	18/10/1993	INSTITUT PASTEUR				
250068 DE 01 ALLEMAGNE	EU939235842	18/10/1993	INSTITUT PASTEUR				
250068 DK 01 DANEMARK	EU939235842	18/10/1993	INSTITUT PASTEUR				
250068 EP 01 DEP.EUROP.	EU939235842	18/10/1993	INSTITUT PASTEUR				
250068 ES 02 DEP.EUROP.	EU040039455	18/10/1993	Division				
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250068 US 01 ETATS-UNIS	US416711	18/10/1993	INSTITUT PASTEUR				
250068 US 02 ETATS-UNIS	US356497	19/07/1999 Division	INSTITUT PASTEUR				
250068 US 03 ETATS-UNIS	US238741	11/09/2002 Continuation	INSTITUT PASTEUR				
250068 US 04 ETATS-UNIS	US294770	15/11/2002 Continuation	INSTITUT PASTEUR				
250068 US 05 ETATS-UNIS	US774602	10/02/2004 Continuation	INSTITUT PASTEUR				

Ss-Dossier 250136 FR 01 AG LSA3 DE P. FALCIPARUM Inventeur: DRU002 DRUILHE PIERRE
N° D.I 194054 AG LSA3 DE P. FALCIPARUM

N° Ss-Dossier	Pays	N° Dépot	Date Dépot	Type de lien	Co-Propriétaire 1	Co-Propriétaire 2	Co-Propriétaire 3
250136 AU 01 AUSTRALIE	BF9507007	13/06/1995	INSTITUT PASTEUR				
250136 CA 01 CANADA	AU6309696	12/06/1996	INSTITUT PASTEUR				
250136 CN 01 CHINA	CN2221029	12/06/1996	INSTITUT PASTEUR				
250136 EP 01 DEP.EUROP.	EU969221076	12/06/1996	INSTITUT PASTEUR				
250136 JP 01 JAPON	JP5027119794	12/06/1996	INSTITUT PASTEUR				
250136 PC 01 PCT	CTFR9600894	12/06/1996	INSTITUT PASTEUR				
250136 US 01 ETATS-UNIS	US973462	12/06/1996	INSTITUT PASTEUR				
250136 US 02 ETATS-UNIS	US742096	20/12/2000 Division	INSTITUT PASTEUR				

Ss-Dossier 250260 US 01 COMPOSES LIPIDO-PEPTIDIQUES Inventeur: DRU002 DRUILHE PIERRE
N° D.I 199044 COMPOSES LIPIDO-PEPTIDIQUES

N° Ss-Dossier Pays	N° Dépot	Date Dépot	Type de lien	Co-Propriétaire 1	Co-Propriétaire 2	Co-Propriétaire 3
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250260 AL 01 ALBANIE	PCTEP0012794	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
250260 AU 01 AUSTRALIE	PCTEP0012794	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
250260 BA 01 BARBADE	PCTEP0012794	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
250260 BG 01 BULGARIE	PCTEP0012794	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
250260 BO 01 BOLIVIE	PCTEP0012794	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
250260 BR 01 BRÉSIL	PCTEP0012794	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
250260 BU 01 BIRMANIE	PCTEP0012794	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
250260 BY 01 BELARUS	PCTEP0012794	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
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250260 CN 01 CHINE POP.	PCTEP0012794	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
250260 CS 01 TCHECOSLOV	PCTEP0012794	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
250260 CU 01 CUBA	PCTEP0012794	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
250260 EF 01 DEF. EUROPE	EU009919747	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
250260 GE 01 GEORGIE	PCTEP0012794	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
250260 GH 01 GHANA	PCTEP0012794	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
250260 HU 01 HONGRIE	PCTEP0012794	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
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250260 IL 01 ISRAEL	PCTEP0012794	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
250260 IN 01 INDE	PCTEP0012794	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
250260 IS 01 ISLANDE	PCTEP0012794	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
250260 JP 01 JAPON	PCTEP0012794	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
250260 KE 01 KENYA	PCTEP0012794	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
250260 KP 01 COREE NORD	PCTEP0012794	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
250260 KR 01 COREE SUD	PCTEP0012794	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
250260 KZ 01 KAZAKHSTAN	PCTEP0012794	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
250260 MA 01 MAROC	PCTEP0012794	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
250260 MG 01 MADAGASCAR	PCTEP0012794	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
250260 MX 01 MEXIQUE	PCTEP0012794	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
250260 MY 01 MALAISIE	PCTEP0012794	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
250260 NZ 01 NZL. ZELAND	PCTEP0012794	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
250260 OA 01 O.A.P.I.	PCTEP0012794	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
250260 PC 01 PCT	PCTEP0012794	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
250260 PH 01 PHILIPPINE	PCTEP0012794	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
250260 PL 01 POLOGNE	PCTEP0012794	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
250260 RO 01 ROUMANIE	PCTEP0012794	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
250260 SG 01 SINGAPOUR	PCTEP0012794	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
250260 SK 01 SARAWAK	PCTEP0012794	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
250260 SL 01 SIER. LEONE	PCTEP0012794	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
250260 SQ 01 SLOVAQUIE	PCTEP0012794	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
250260 SU 01 FED. RUSSIE	PCTEP0012794	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
250260 TH 01 THAILANDE	PCTEP0012794	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
250260 TK 01 TURKIE	PCTEP0012794	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
250260 TR 01 TURQUIE	PCTEP0012794	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
250260 US 03 ETATS-UNIS	US161760	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
250260 VN 01 VIET-NAM	PCTEP0012794	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
250260 YU 01 CROATIE	PCTEP0012794	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	
250260 ZA 01 AFRIQUE SUD	PCTEP0012794	8/12/2000		INSTITUT PASTEUR	UNIVERSITE DE LIL	

Ss-Dossier 250260 US 02 COMPOSES LIPIDO-PEPTIDIQUES

N° D.I 199044 COMPOSES LIPIDO-PEPTIDIQUES

Inventeur: DRU002 DRUILLE PIERRE

N° Ss-Dossier Pays	N° Dépot	Date Dépot	Type de lien	Co-Propriétaire 1	Co-Propriétaire 2	Co-Propriétaire 3
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Ss-Dossier 250260 US 04 COMPOSES LIPIDO-PEPTIDIQUES

Inventeur: DRU002 DRUILLE PIERRE

S8-Dossier 250300 EP 01 LSA 3 et adjuvants

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Ss-Dossier	250322 CA 01 Antigènes de Plasmodium falciparum	Inventeur: DRUO02 DUYLIE PIERRE
N° D.I	201031 Antigènes de Plasmodium falciparum	
N° Sg-Dossier	Bayer	Date Dépot
N° Sg-Dossier	Bayer	Date Dépot
		Tout de bien
		Co-Propriétaire 1 Co-Propriétaire 2 Co-Propriétaire 3

CAN345206	16/05/2001	INSTITUT PASTEUR
250322 AL 01 ALBANIE	15/05/2002	INSTITUT PASTEUR
250322 AU 01 AUSTRALIE	15/05/2002	INSTITUT PASTEUR
250322 BB 01 BARBADE	15/05/2002	INSTITUT PASTEUR
250322 BG 01 BULGARIE	15/05/2002	INSTITUT PASTEUR
250322 BO 01 BOLIVIE	15/05/2002	INSTITUT PASTEUR
250322 BR 01 BRASIL	15/05/2002	INSTITUT PASTEUR
250322 BU 01 BIRMANIE	15/05/2002	INSTITUT PASTEUR
250322 BY 01 BELARUS	15/05/2002	INSTITUT PASTEUR
250322 CA 03 CANADA	15/05/2002	INSTITUT PASTEUR
CAN382977	15/05/2002	INSTITUT PASTEUR
250322 CN 01 CHINE POP.	15/05/2002	INSTITUT PASTEUR
250322 CS 01 TCHECOSLOV	15/05/2002	INSTITUT PASTEUR
250322 CU 01 CUBA	15/05/2002	INSTITUT PASTEUR
250322 EP 01 DEB. EUROP.	15/05/2002	INSTITUT PASTEUR
EU027328723	15/05/2002	INSTITUT PASTEUR
250322 GE 01 GEORGIE	15/05/2002	INSTITUT PASTEUR
250322 GH 01 GHANA	15/05/2002	INSTITUT PASTEUR
250322 HU 01 HONGRIE	15/05/2002	INSTITUT PASTEUR
250322 ID 01 INDONESIE	15/05/2002	INSTITUT PASTEUR
250322 IL 01 ISRAEL	15/05/2002	INSTITUT PASTEUR
250322 IN 01 INDE	15/05/2002	INSTITUT PASTEUR
250322 IS 01 ISLANDE	15/05/2002	INSTITUT PASTEUR
250322 JP 01 JAPON	15/05/2002	INSTITUT PASTEUR
250322 KE 01 KENYA	15/05/2002	INSTITUT PASTEUR
250322 KR 01 CORÉE NORD	15/05/2002	INSTITUT PASTEUR
250322 KP 01 CORÉE SUD	15/05/2002	INSTITUT PASTEUR
250322 KZ 01 KAZAKHSTAN	15/05/2002	INSTITUT PASTEUR
250322 MA 01 MAROC	15/05/2002	INSTITUT PASTEUR
250322 MG 01 MADAGASCAR	15/05/2002	INSTITUT PASTEUR
250322 MK 01 MEXIQUE	15/05/2002	INSTITUT PASTEUR
250322 MY 01 MALAISIE	15/05/2002	INSTITUT PASTEUR
250322 NZ 01 NVL. ZELAND	15/05/2002	INSTITUT PASTEUR
250322 OA 01 O.A.P. I.	15/05/2002	INSTITUT PASTEUR
250322 PC 01 PCT	15/05/2002	INSTITUT PASTEUR
250322 PH 01 PHILIPPINE	15/05/2002	INSTITUT PASTEUR
250322 PL 01 POLOGNE	15/05/2002	INSTITUT PASTEUR
250322 RO 01 ROUMANIE	15/05/2002	INSTITUT PASTEUR
250322 SG 01 SINGAPOUR	15/05/2002	INSTITUT PASTEUR
250322 SK 01 SLOVAQUIE	15/05/2002	INSTITUT PASTEUR
250322 SL 01 SLOVÉNIE	15/05/2002	INSTITUT PASTEUR
250322 SR 01 SERBIE	15/05/2002	INSTITUT PASTEUR
250322 ST 01 S. TOME ET PR.	15/05/2002	INSTITUT PASTEUR
250322 SV 01 SUÈDE	15/05/2002	INSTITUT PASTEUR
250322 SW 01 SUISSE	15/05/2002	INSTITUT PASTEUR
250322 TH 01 THAÏLANDE	15/05/2002	INSTITUT PASTEUR
250322 TR 01 TURQUIE	15/05/2002	INSTITUT PASTEUR
250322 UA 01 UKRAÏNE	15/05/2002	INSTITUT PASTEUR
250322 US 01 ETATS-UNIS	15/05/2002	INSTITUT PASTEUR
250322 VE 01 VENEZUELE	15/05/2002	INSTITUT PASTEUR
250322 VN 01 VIETNAM	15/05/2002	INSTITUT PASTEUR
250322 YU 01 YOUGOSLAVIE	15/05/2002	INSTITUT PASTEUR
250322 ZW 01 ZAMBIE	15/05/2002	INSTITUT PASTEUR

Ss-Dossier		250322 CA 02	Antigènes de Plasmodium falciparum		Inventeur: DRU002 DRUILHE PIERRE				
No Ss-Dossier		No P.1 201031	Antigènes de Plasmodium falciparum		Co-Propriétaire 1				
No	Ss-Dossier	Date	Dépôt	Type de lien	Date	Dépôt			
250322	SQ 01 SLOVAQUIE	PCTFR0201637	15/05/2002	INSTITUT PASTEUR	250322	SA 01 SLOVAQUIE	PCTFR0201637	15/05/2002	INSTITUT PASTEUR
250322	SU 01 FED RUSSIE	PCTFR0201637	15/05/2002	INSTITUT PASTEUR	250322	SH 01 THAILANDE	PCTFR0201637	15/05/2002	INSTITUT PASTEUR
250322	TH 01 THAILANDE	PCTFR0201637	15/05/2002	INSTITUT PASTEUR	250322	TK 01 TRANSKEI	PCTFR0201637	15/05/2002	INSTITUT PASTEUR
250322	TK 01 TRANSKEI	PCTFR0201637	15/05/2002	INSTITUT PASTEUR	250322	TN 01 TUNISIE	PCTFR0201637	15/05/2002	INSTITUT PASTEUR
250322	TN 01 TUNISIE	PCTFR0201637	15/05/2002	INSTITUT PASTEUR	250322	TR 01 TURQUIE	PCTFR0201637	15/05/2002	INSTITUT PASTEUR
250322	TR 01 TURQUIE	PCTFR0201637	15/05/2002	INSTITUT PASTEUR	250322	US 01 ETATS-UNIS	US712533	15/05/2002	INSTITUT PASTEUR
250322	US 01 ETATS-UNIS	US712533	15/05/2002	INSTITUT PASTEUR	250322	VN 01 VIET-NAM	PCTFR0201637	15/05/2002	INSTITUT PASTEUR
250322	VN 01 VIET-NAM	PCTFR0201637	15/05/2002	INSTITUT PASTEUR	250322	YU 01 CROATIE	PCTFR0201637	15/05/2002	INSTITUT PASTEUR
250322	YU 01 CROATIE	PCTFR0201637	15/05/2002	INSTITUT PASTEUR	250322	ZA 01 AFRIQUE SUD	PCTFR0201637	15/05/2002	INSTITUT PASTEUR
250322	ZA 01 AFRIQUE SUD	PCTFR0201637	15/05/2002	INSTITUT PASTEUR					
250322	AL 01 ALBANIE	PCTFR0201637	23/05/2001	INSTITUT PASTEUR					
250322	AL 01 ALBANIE	PCTFR0201637	15/05/2002	INSTITUT PASTEUR					
250322	AU 01 AUSTRALIE	PCTFR0201637	15/05/2002	INSTITUT PASTEUR					
250322	BB 01 BARBADE	PCTFR0201637	15/05/2002	INSTITUT PASTEUR					
250322	BG 01 BULGARIE	PCTFR0201637	15/05/2002	INSTITUT PASTEUR					
250322	BO 01 BOLIVIE	PCTFR0201637	15/05/2002	INSTITUT PASTEUR					
250322	BR 01 BRESIL	PCTFR0201637	15/05/2002	INSTITUT PASTEUR					
250322	BU 01 BIRMANIE	PCTFR0201637	15/05/2002	INSTITUT PASTEUR					
250322	BY 01 BELARUS	PCTFR0201637	15/05/2002	INSTITUT PASTEUR					
250322	CA 03 CANADA	CA2382977	15/05/2002	INSTITUT PASTEUR					
250322	CN 01 CHINE POP.	PCTFR0201637	15/05/2002	INSTITUT PASTEUR					
250322	CS 01 TCHECOSLOV	PCTFR0201637	15/05/2002	INSTITUT PASTEUR					
250322	CU 01 CUBA	PCTFR0201637	15/05/2002	INSTITUT PASTEUR					
250322	EP 01 REP. EUROPE	EU07328723	15/05/2002	INSTITUT PASTEUR					
250322	GE 01 GEORGIE	PCTFR0201637	15/05/2002	INSTITUT PASTEUR					
250322	GH 01 GHANA	PCTFR0201637	15/05/2002	INSTITUT PASTEUR					
250322	HU 01 HONGRIE	PCTFR0201637	15/05/2002	INSTITUT PASTEUR					
250322	ID 01 INDONESIE	PCTFR0201637	15/05/2002	INSTITUT PASTEUR					
250322	IL 01 ISRAEL	PCTFR0201637	15/05/2002	INSTITUT PASTEUR					
250322	IN 01 INDE	PCTFR0201637	15/05/2002	INSTITUT PASTEUR					
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250322	JP 01 JAPON	PCTFR0201637	15/05/2002	INSTITUT PASTEUR					
250322	KE 01 KENYA	PCTFR0201637	15/05/2002	INSTITUT PASTEUR					
250322	KP 01 COREE NORD	PCTFR0201637	15/05/2002	INSTITUT PASTEUR					
250322	KR 01 COREE SUD	PCTFR0201637	15/05/2002	INSTITUT PASTEUR					
250322	KZ 01 KAZAKHSTAN	PCTFR0201637	15/05/2002	INSTITUT PASTEUR					
250322	MA 01 MAROC	PCTFR0201637	15/05/2002	INSTITUT PASTEUR					
250322	MG 01 MADAGASCAR	PCTFR0201637	15/05/2002	INSTITUT PASTEUR					
250322	MX 01 MEXIQUE	PCTFR0201637	15/05/2002	INSTITUT PASTEUR					
250322	MY 01 MALAISIE	PCTFR0201637	15/05/2002	INSTITUT PASTEUR					
250322	NZ 01 NVL. ZELAND	PCTFR0201637	15/05/2002	INSTITUT PASTEUR					
250322	OA 01 O. A. P.	PCTFR0201637	15/05/2002	INSTITUT PASTEUR					
250322	PC 01 PCT	PCTFR0201637	15/05/2002	INSTITUT PASTEUR					
250322	PH 01 PHILIPPINE	PCTFR0201637	15/05/2002	INSTITUT PASTEUR					
250322	PL 01 POLOGNE	PCTFR0201637	15/05/2002	INSTITUT PASTEUR					
250322	RO 01 ROUMANIE	PCTFR0201637	15/05/2002	INSTITUT PASTEUR					
250322	SG 01 SINGAPOUR	PCTFR0201637	15/05/2002	INSTITUT PASTEUR					
250322	SK 01 SARKAWAK	PCTFR0201637	15/05/2002	INSTITUT PASTEUR					
250322	SL 01 SIER. LEONE	PCTFR0201637	15/05/2002	INSTITUT PASTEUR					
250322	SQ 01 SLOVAQUIE	PCTFR0201637	15/05/2002	INSTITUT PASTEUR					
250322	SU 01 FED RUSSIE	PCTFR0201637	15/05/2002	INSTITUT PASTEUR					
250322	TH 01 THAILANDE	PCTFR0201637	15/05/2002	INSTITUT PASTEUR					

250322 TK 01 TRANSKEI	PCTFR0201637	15/05/2002	INSTITUT PASTEUR
250322 TN 01 TUNISIE	PCTFR0201637	15/05/2002	INSTITUT PASTEUR
250322 TR 01 TURQUIE	PCTFR0201637	15/05/2002	INSTITUT PASTEUR
250322 US 01 ETATS-UNIS	US712533	15/05/2002	INSTITUT PASTEUR
250322 VN 01 VIET-NAM	PCTFR0201637	15/05/2002	INSTITUT PASTEUR
250322 XU 01 CROATIE	PCTFR0201637	15/05/2002	INSTITUT PASTEUR
250322 ZA 01 AFRIQUE SUD	PCTFR0201637	15/05/2002	INSTITUT PASTEUR
Ss-Dossier 250322 CA 04 Antigènes de Plasmodium falciparum			
N° D.I 201031 Antigènes de Plasmodium falciparum		Inventeur: DRU002 DRUILHE PIERRE	
N° Ss-Dossier Pays	N° Dépôt	Date Dépôt	Type de lien
-----	-----	15/05/2002	Co-Propriétaire 1 Co-Propriétaire 2 Co-Propriétaire 3
-----	CANADA CA2382977	15/05/2002	INSTITUT PASTEUR
Ss-Dossier 250369 GB 01 Anticorps recombinants de P.falciparum			
N° D.I 202046 Anticorps recombinants de P.falciparum		Inventeur: DRU002 DRUILHE PIERRE	
N° Ss-Dossier Pays	N° Dépôt	Date Dépôt	Type de lien
-----	-----	16/08/2001	Co-Propriétaire 1 Co-Propriétaire 2 Co-Propriétaire 3
-----	GR.BRETAG. GB010200575	16/08/2001	DANISH TECHNOLOGI INSTITUT PASTEUR
250369 AU 01 AUSTRALIE	AU2002326106	16/08/2002	DANISH TECHNOLOGI INSTITUT PASTEUR
250369 BR 01 BRESIL	BR02119439	16/08/2002	DANISH TECHNOLOGI INSTITUT PASTEUR
250369 CA 01 CANADA	CA2458890	16/08/2002	DANISH TECHNOLOGI INSTITUT PASTEUR
250369 EP 01 REP.EUROP.	EU027605138	16/08/2002	DANISH TECHNOLOGI INSTITUT PASTEUR
250369 JP 01 JAPON	JP2003-521275	16/08/2002	DANISH TECHNOLOGI INSTITUT PASTEUR
250369 PC 01 PCT	PCTIB0203995	16/08/2002	DANISH TECHNOLOGI INSTITUT PASTEUR
250369 US 01 ETATS-UNIS	US486703	16/08/2002	DANISH TECHNOLOGI INSTITUT PASTEUR
Ss-Dossier 250381 US 01 Composition immunogène dérivée de MSP3			
N° D.I 202101 Composition immunogène dérivée de MSP3		Inventeur: DRU002 DRUILHE PIERRE	
N° Ss-Dossier Pays	N° Dépôt	Date Dépôt	Type de lien
-----	-----	15/11/2002	Co-Propriétaire 1 Co-Propriétaire 2 Co-Propriétaire 3
-----	ETATS-UNIS US294770	15/11/2002	INSTITUT PASTEUR
Ss-Dossier 250424 EP 01 Antibodies effective at killing P.falci			
N° D.I 203044 Antibodies effective at killing P.falci.		Inventeur: DRU002 DRUILHE PIERRE	
N° Ss-Dossier Pays	N° Dépôt	Date Dépôt	Type de lien
-----	-----	24/10/2003	Co-Propriétaire 1 Co-Propriétaire 2 Co-Propriétaire 3
-----	REP.EUROP. EP03296735	24/10/2003	INSTITUT PASTEUR
250424 PC 01 PCT	PCTEP2004012909	22/10/2004	INSTITUT PASTEUR
Ss-Dossier 250426 US 01 MSP-3 GLURP malaria vaccine candidate			
N° D.I 203080 MSP-3 GLURP malaria vaccine candidate		Inventeur: DRU002 DRUILHE PIERRE	
N° Ss-Dossier Pays	N° Dépôt	Date Dépôt	Type de lien
-----	-----	24/10/2003	Co-Propriétaire 1 Co-Propriétaire 2 Co-Propriétaire 3
-----	ETATS-UNIS US691672	24/10/2003	INSTITUT PASTEUR
250426 PC 01 PCT	PCTEP2004012910	22/10/2004	INSTITUT PASTEUR
Ss-Dossier 250431 EP 01 Nouvel antigène de P.falciparum : LSA-5			
N° D.I 203034 Nouvel antigène de P.falciparum : LSA-5		Inventeur: DRU002 DRUILHE PIERRE	
N° Ss-Dossier Pays	N° Dépôt	Date Dépôt	Type de lien
-----	-----	15/12/2003	Co-Propriétaire 1 Co-Propriétaire 2 Co-Propriétaire 3
-----	REP.EUROP. EU032931586	15/12/2003	INSTITUT PASTEUR
Ss-Dossier 250431 PC 01 Nouvel antigène de P.falciparum : LSA-5			
N° D.I 203034 Nouvel antigène de P.falciparum : LSA-5		Inventeur: DRU002 DRUILHE PIERRE	
N° Ss-Dossier Pays	N° Dépôt	Date Dépôt	Type de lien
-----	-----	15/12/2004	Co-Propriétaire 1 Co-Propriétaire 2 Co-Propriétaire 3
-----	PCTEP2004014848	15/12/2004	INSTITUT PASTEUR

Ss-Dossier	250435	EP 01	Modèle souris	Inventeur:	DRU002	DRUILHE PIERRE
N° D.I	203134		Development of an improved mouse model			
N° Ss-Dossier Pays		N° Dépot	Date Dépot	Type de lien		
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250435	PC 01	PCT	7/01/2005			INSTITUT PASTEUR
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						INSTITUT PASTEUR
Ss-Dossier	250453	EP 01	Major improvement in human hepatocytes	Inventeur:	DRU002	DRUILHE PIERRE
N° D.I	203100		Major improvement in human hepatocytes			
N° Ss-Dossier Pays		N° Dépot	Date Dépot	Type de lien		
-----	---	---	9/01/2004			Co-Propriétaire 1 Co-Propriétaire 2 Co-Propriétaire 3
250453	PC 01	PCT	7/01/2005			INSTITUT PASTEUR INSERM
						INSTITUT PASTEUR INSERM
						INSTITUT PASTEUR INSERM
Ss-Dossier	250458	US 01	Antibodies against malaria	Inventeur:	DRU002	DRUILHE PIERRE
N° D.I	204076		Antibodies against malaria			
N° Ss-Dossier Pays		N° Dépot	Date Dépot	Type de lien		
-----	---	---	2/08/2004			Co-Propriétaire 1 Co-Propriétaire 2 Co-Propriétaire 3
						INSTITUT PASTEUR

** Fin d'édition **